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TUMORS OF DOMESTIC ANIMALS

By

ROBERT J. FORMAD, Associate Pathologist, Pathological Division
Bureau of Animal Industry

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By Robert J. Formad, *Associate Pathologist, Pathological Division, Bureau of Animal Industry*

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INTRODUCTION

A tumor is an atypical, abnormal growth of tissue, developing without apparent cause, having no function, and growing independently of the laws that govern the growth of the body. Until the true cause of tumors is known no satisfactory definition can be given, as can be seen from the fact that every prominent authority on tumors has given a different definition of a tumor, depending on the particular angle from which his studies were undertaken.

Tumors are comparatively common in the domestic animals. They are of considerable interest to the veterinary practitioner and of more

or less economic importance to the livestock owner. Their presence in the meat-producing animals is of even greater significance to the veterinary inspector in the abattoir, who passes on the wholesomeness of about two-thirds of the meat products consumed in the United States. The inspector on the killing floor observes the animal after slaughter and consequently renders his decision from the macroscopic or gross appearance of the lesions. A definite decision can not always be made as to the particular type of tumor found on post-mortem inspection, and consequently many tumors of various types are forwarded to the laboratory for a definite diagnosis. This bulletin discusses tumors of domestic animals chiefly from the standpoint of macroscopic examination of the structure.

The word "tumor" means a swelling, but every swelling is not a tumor. Inflammation processes, infections by microorganisms, and other agencies may produce swellings which are not true tumors. It is often difficult to draw a sharp line of distinction between some inflammatory swellings and tumors. A swelling produced by inflammation persists as long as the cause producing it lasts and disappears when the cause subsides. A tumor when once started to develop continues to grow independently of the surrounding tissue of its host. Tumors continue to increase in size even when the host becomes emaciated. Age and sex are no barriers to the growth of tumors. This independence of tumors is designated by some writers as lawlessness or anarchy of growth and is the result of the increase in the number of its component elements; hence the names "new growth," "new formation," "neoplasm," and "pseudoplasm" are used. These terms mean the multiplication and growth of certain cells and serve to differentiate a true tumor from an ordinary swelling. The more definite term "neoplasm" will be used extensively in this bulletin in place of tumor.

A neoplasm may remain at its original site, the starting point of development, and form a primary growth. Later small particles of the neoplasm may become detached, enter the blood stream or the lymph stream, and be carried to different parts of the body until finally lodged, when they form secondary or daughter neoplasms. This transmission of the detached particles of the primary neoplasm to new locations is known as metastasis. This constitutes the lawlessness of neoplasms, as the secondary metastatic growths, having migrated to a new locality, start an independent existence by forming secondary neoplasms identical in structure with the primary tumor. Primary as well as secondary neoplasms may interfere with the function of an organ by mechanical compression of the blood supply. For example, when a neoplasm is situated in the cranial cavity or in the spinal canal, pressure lesions may eventually cause paralysis.

ETIOLOGY

The cause of neoplasms is still unknown, notwithstanding the vast amount of literature on the subject and all the research done on neoplasms, especially cancers. Various theories have been suggested, but they all remain hypotheses that account for individual neoplasms only, failing, however, to explain the causation of all neoplasms. The recognized theories of the etiology of neoplasm formation are stated in the paragraphs that follow.

THE CONSTITUTIONAL DYSCRASIA OR DIATHESIS THEORY

The older writers, including Billroth (*2*),[1] advanced the view that a diseased state of the fluids in the body bring about a constitutional dyscrasia, which acts as a predisposing cause in the formations of neoplasms. This diseased state or predisposition was either acquired or inherited. This hypothesis was also advocated by the champions of the hereditary origin of neoplasms before the minute structure of tissues was known.

THE MECHANICAL OR IRRITATION THEORY

With the advent of the cell doctrine, the proliferative activity of cells in response to external irritation of a part gave rise to the mechanical theory advocated by Virchow (*21*) and his followers as the cause of neoplasms. Persistent and long irritation of a part appears to be a reasonable explanation of some epithelial neoplasms. Epithelioma on the lip in pipe smokers, epithelioma of the tongue from the irritation of caries of the teeth, carcinoma of the testicle in chimney sweeps, and carcinoma and sarcoma of the breast—all these have been attributed to irritation resulting from injuries. On the other hand the iron bit of a much-abused horse, the ring in the muzzle of a bull, the vicious punishment of the pugilist, and the violent injuries of the football player are never mentioned as the cause of neoplasms. It is therefore possible that injuries and irritation may be coincidental with some unknown, underlying cause acting at the same time.

THE "EMBRYONAL RESTS" OR PREFORMATION THEORY

Cohnheim (*4*) attributed the development of neoplasm to misplacement of fragments of embryonic tissue in early embryonal life before the differentiation of any of the organs was completed. The misplaced fragments or embryonal rests lie dormant or sequestered in different parts of the body until favorable conditions or physiological stimuli bring about their development by subsequent sprouting and growth. No other theory could account for the presence of hair, bone, cartilage, and teeth in the dermoid cysts, or the conglomeration of various tissues in the mixed neoplasms of the parotid gland and those in the ovary and in the suprarenal gland. Although the theory of embryonal rest is valuable to explain these freaks or unusual structures in neoplasms, it does not explain the ordinary types of neoplasms.

Ribbert (*17*) advanced a modified embryonal theory. He supposes that certain changes must precede in the tissue, preparing a favorable soil, before the embryonic rests can start to grow. These changes are the product of certain agents elaborated by the tissue surrounding the embryonic rests bringing about a "disturbance of tissue tension."

Hauser (*8*, *9*) and his followers maintained the view that the changes within the cells of the embryonic rest, rather than the changes in the surrounding tissues, must take place to produce a new race of cells which are larger in size with a larger nucleus, containing more chromatin, and endowed with a greater property for repro-

[1] Numbers in parentheses in italics refer to "Literature cited," p. 39.

duction. Hauser thus considers the changes in the cells more important than Ribbert's disturbance of tissue tension.

Von Hansemann (*7*) went even further, considering the increased growth energy of cells due to a gain in the power of independence and coincidental loss of differentiation of chromatin, brought about by chromatic changes in the nucleus with unequal division of chromosomes.

THE THEORY OF NERVOUS INFLUENCE

Disturbance of trophic innervation has been ascribed as the cause of neoplasms, the overgrowth of tissue being the result of local irregularities of nervous influence, particularly in neoplasms that are of nerve origin, formed in the course of nerve trunks. It would be difficult to conceive of the formation of all neoplasms as due to such a cause.

THE PARASITIC THEORY

The parasitic theory accepted in the Middle Ages was revived some time ago, especially by investigators of cancer, but this hypothesis has received less credence than other theories. Protozoanlike bodies with marked degenerative changes of the cells have been found in neoplasms by Thomas (*20*), Russell (*18*), Gaylord (*6*), von Podwyssozki (*16*), and others. This, however, indicates only their accidental presence in a favorable soil produced by the degenerative changes and the accompanying chronic irritation, but throws no light on the causation of neoplasms; moreover, none of these observers describe exactly the same bodies that they consider as protozoan parasites.

In line with the advocates of the parasitic theory are such investigators as Scheurlen (*19*), Doyen (*5*), and others, who have found bacteria in neoplasms and described the *Bacillus neoformans* as the cause of cancer. The "Plimmer bodies," which are of blastomycetic origin, are said by Plimmer (*15*) to be the cause of cancer.

One of the principal objections to the parasitic theory of neoplasms is the difficulty of reproducing the disease by transplantation of fragments of neoplasms of one animal to an animal of another species.

Late experiments by Jensen (*10*), Loeb (*12*), and others in the transplantation of tissues have been successfully carried out, but these experiments prove only that the cells of malignant neoplasms of an animal can be transplanted at times to another animal of the same sort and continue to live and grow in the same fashion that a metastatic growth forms a secondary neoplasm. They do not prove the parasitic nature of neoplasms, because in most of them neither protozoa nor bacteria can be found. Benign neoplasms can not be transplanted.

CLASSIFICATION OF NEOPLASMS

Up to the present time no classification embracing all neoplasms has been accepted as satisfactory. Neoplasms may be classified clinically as to their nature, histogenetically as to their structure, or morphologically as to their shape.

CLASSIFICATION BY NATURE (CLINICAL CLASSIFICATION)

Clinically neoplasms are divided into two classes, benign and malignant.

Benign neoplasms are usually harmless and in themselves do not endanger life except by accidental location. They grow slowly from the center and mechanically push aside the surrounding tissues and remain distinct from them. Their slow growth permits a reaction of the surrounding tissues to concentrate around the neoplasm to form a capsule which sharply defines the neoplasm from the surrounding tissue. Even when diffused, benign neoplasms do not infiltrate the surrounding tissues and their growth may be arrested, to be renewed later. The paucity of their cells may account for their slow growth. Though usually small, they may become rather large in certain localities, as, for example, lipomas in the abdominal cavity and myomas in the uterus. They do not recur after complete removal; neither does metastasis occur.

Benign neoplasms, though harmless in their nature, may produce death indirectly by accidental location if in or contiguous to vital organs. A benign neoplasm of the larynx may become lodged between the vocal cords and completely obstruct respiration; when developed in the brain or the spinal cord it produces paralysis by pressure and eventually may lead to death. Benign neoplasms may interfere with the nutrition of vital organs either by pressure, thus limiting the blood supply of the latter, or by obstructing the digestive tract, bringing about a state of ill health commonly referred to as cachexia, resulting in emaciation or even starvation.

Malignant neoplasms are always harmful and usually destroy life in whatever situation they arise. Because of their preponderance in cells and a richer blood supply they grow more rapidly than benign neoplasms. They are frequently softer in consistence and usually have no capsule and are ill defined from the surrounding tissues. They increase by peripheral extension and dissemination of the proliferating cells into the surrounding tissues. They give metastases to internal organs by either the blood vessels, as is the case in sarcomas, or the lymph vessels, which is the common mode of cancer metastasis. They usually recur after removal.

The prominent features of malignancy in neoplasms are metastases, infiltration of the surrounding tissues, and recurrence. Metastasis may take place by direct contact, which is rare but is sometimes observed in neoplasms of the mucous membranes, or by the transmission of particles of the primary growth through the blood or lymph vessels, which is the usual mode of metastasis. These particles in the blood or lymph stream ultimately lodge in either proximate or distal parts of the body, where they grow rapidly in their new environment and deprive the tissues of some of the nutrition by appropriating blood enough for their own existence. Neoplasms when situated near a blood vessel may, during their growth, diminish by pressure the blood supply of an organ and interfere with its functional activity. The entrance of neoplastic elements into the vascular channels is the result of the destructive nature of a malignant neoplasm and is comparable to embolism. Anemia of the organ usually results and may eventually be followed by general anemia of the body, and in the more severe cases by emaciation and cachexia.

The peripheral cells in malignant neoplasms proliferate more rapidly and receive more nourishment from the surrounding tissues than the cells in the interior of the neoplasm. Insufficient nutrition and increased pressure, to which the inner portion is subjected, bring about degenerative changes which are followed by atrophy and absorption of the inner portion of the neoplasm, resulting in the formation of a cavity. The cavity may contain remnants of the degenerated product, or may be filled with an albuminous fluid or serum resulting from negative pressure.

Marked anemia, emaciation or wasting of the body and extreme cachexia are invariably associated with malignant neoplasms (cancers) of the esophagus or the stomach, which interfere with the passage of food, resulting in starvation; some malignant neoplasms (sarcomas) in other locations, though larger in size, may not produce such marked cachexia.

Superficial malignant neoplasms often ulcerate around their periphery. The ulceration may be accompanied by inflammatory changes and offers a favorable soil for bacterial infection, and inflammation. These processes, singly or collectively, may produce soluble substances which are absorbed into the circulation and contribute largely in bringing about cachexia.

Chemical analysis of neoplasms has shown that their composition closely approximates the composition of the structures from which they grow. Glycogen has been found in excess in neoplasms which originated in tissues that normally contain glycogen. Enzymes are likewise present in greater quantity in certain neoplasms than in the normal tissues from which they grow.

During the last few years pathological chemistry has been actively used in research of neoplasms in human-cancer investigations and in the transplantation experiments of malignant neoplasms.

Malignant neoplasms differ in their rapidity of growth, depending on the location and the blood supply of the tissue. They also differ in the extent of their metastatic ability. Some are more prone to metastasis than others, the latter expressing their malignancy by peripheral invasion of the surrounding tissues. Recurrence, which is the chief feature of malignant neoplasms, is also variable, depending on the difference in type. Under exceptional circumstances malignant neoplasms have been known to revert or undergo apparently spontaneous retrogression, resulting in their complete disappearance.

Degenerative changes in benign as well as in malignant neoplasms are very common. Any degeneration that affects an organ or a tissue may likewise affect a neoplasm, as albuminous, fatty, mucoid, or colloid degeneration. Calcification, pigmentation, glycogenous infiltration, necrotic changes, and hemorrhages may also be observed in neoplasms.

CLASSIFICATION BY STRUCTURE (HISTOGENETIC CLASSIFICATION)

The histogenetic classification of neoplasms is based on the structural elements of which the neoplasms are made up. This classification was suggested by Virchow (*21*) after the development of the cell doctrine and the fact that the animal body is composed of ele-

mentary tissue, which forms every structure, organ, or system of the body.

Virchow's classification is as follows:

1. Histoid. Simple-tissue neoplasms.
2. Organoid. Compound-tissue neoplasms consisting of several tissues like those found in organs.
3. Teratoid. Mixed or congenital new formations, containing such structures as teeth, hair, cartilage, and bone.

The following modified histogenetic classification is used by many authorities:

1. Connective-tissue neoplasms.
2. Epithelial neoplasms.
3. Teratoid neoplasms.

Adami (*1*) has suggested a modification of the histogenetic classification based on embryonic layer formation, as follows:

1. The lepidic group or lepidomas, comprising the lining membrane tissues or rind neoplasms, which are of epithelial and mesothelial structures deficient in stroma.
2. The hylic or primitive pulp tissues of undifferentiated material, which are rich in stroma comprising essentially hypoblastic and mesoblastic structures.

A careful study of the minute structure of neoplasms shows that all neoplasms are composed of elements present in the animal body in their adult or in their embryonal state. Neoplasms therefore originate from existing elements in the animal body and reproduce the adult or the embryonal tissue from which they have originated. Neoplasms, like normal tissues, consist of cells and a supporting interstitial ground substance. The cells of neoplasms, although retaining the morphological type of normal tissues sufficiently to be recognizable, are subject to considerable variation in size and shape. The greater their departure from adult cells the more pronounced becomes the embryonal type of structure. The stroma is more abundant in neoplasms which originate from the mesoderm than in the neoplasms originating from the ectoderm or the entoderm, which have a very scanty stroma.

When a neoplasm is composed of a single tissue which is analogous to the tissue from which it started, it is known as a homologous growth, whereas those neoplasms which have departed from the normal tissue are described as heterologous.

The histogenetic classification is followed in the arrangement of this bulletin and the various kinds of neoplasms in each class are discussed in order of their frequency of occurrence.

CLASSIFICATION BY SHAPE (MORPHOLOGICAL CLASSIFICATION)

Morphological classification is used to distinguish neoplasms by macroscopic conformation before the actual structure and nature are determined. It is as follows:

1. Uniform swelling (affecting organs): Goiter, lymphoma.
2. Flat tabular swelling (slight elevations above the surface): Keloid angioma, epithelioma, sarcoma of serous membranes.
3. Nodes growing centrally which lie embedded in the tissue: Fibroma, myoma, adenoma.
4. Nodes growing peripherally: Primary sarcoma, primary carcinoma.
5. Tubers (partly protruding nodes): Chondroma, osteoma, osteosarcoma.
6. Fungus (spongy growth): Telangiectatic sarcoma, cavernous angioma.

7. Polyps (pedunculated growth) : Myoma, soft fibroma, sometimes also lipoma, adenoma.
8. Papillæ (dermic growth) : Corns, cutaneous horns.
9. Dendrites (branching or cauliflowerlike growth) : Warts, papilloma, epithelioma.
10. Cysts (saclike or bladderlike neoplasms) : Glandular cystoma, papillary cystoma.

NOMENCLATURE

In naming a neoplasm the root word of the tissue of which the neoplasm is composed is used with the addition of the Greek word "oma," signifying tumor or neoplasm. Thus the names fibroma, myoma, osteoma, neuroma, angioma, and other similar ones are obtained. An exception is made in naming a group of neoplasms, which from their resemblance to flesh (sarko) are known as sarcomas, and also in designating another group of neoplasms, having the fanciful resemblance to a crab (karkinos), are called carcinomas.

CONNECTIVE-TISSUE NEOPLASMS

FIBROMA

Definition.—A fibroma is composed of fibrous connective tissue, which it resembles in structure and arrangement, but presents some differences in its finer composition. Originating from the mesoderm, the connective tissue has a wide distribution and a marked difference in the arrangement and grouping of the fibers. The bundles may be arranged loosely, as in the areolar tissue and in the submucous tissue in mucous membranes, or the bundles may be very compactly arranged, as in the periosteum, fascias, and tendons.

Seats.—The wide distribution of connective tissue makes it possible for fibromas to start and grow in any part of the body, but there are certain places in which they grow with preference. Some of the more common places are the skin and the subcutaneous connective tissues of the chest. Fibromas are often found in the chests of horses and in the dewlaps of cows.

They may be found at times in the region of the throat and neck in cattle and horses as well as in other animals. The extremities, especially about the knee and elbow, are comparatively common places to find fibromas in cattle, horses, and dogs. The tail in cattle is also a frequent seat of hard fibromas. Care must be taken, however, to differentiate the hard, fibromatous nodules on the tail from nodular formations which may be tuberculous or actinomycotic in nature.

Less frequently fibromas are found in other locations, as the "fibroma diffusum" involving the muzzle of cattle, where it may become as extensive in size as the muzzle itself. Polypoid or pedunculated fibromas are found in the nose, pharynx, and larynx in cattle and horses. In the latter locations they have been known to cause fatal results by obstructing respiration. Other sites for polypoid fibromas are the uterus, vagina, and ovary in cows, mares, and bitches. In these latter localities the neoplasm assumes a more pedunculated shape, is harder, and may be many times larger than the comparatively small, soft, edematous nasal polypi. The tongue is also one of the rare seats of fibroma. The tumor usually grows near the upper surface without encroachment on the mucous mem-

brane, is dense, hard, white, and well defined from the muscle of the tongue. Fibroma in the tongue should be differentiated from actinomycosis, which often has collections of pus, sulphur-colored granules of colonies of actinomyces, and calcified areas. Among the rare locations for fibroma are the esophagus, stomach, intestine, mammary gland, lung, liver, kidney, and spleen.

Structure.—According to the dense or loose arrangement of the fibrous-tissue bundles, fibromas are designated as soft or hard. They may be found in any part of the body where connective tissue is naturally present. A fibroma grows comparatively slowly and is encapsulated and usually poorly supplied with lymph and blood vessels. Exceptionally a fibroma may be very vascular, as the bleeding fibroids, which occur in man, but they are rare in animals. Fibromas are usually single, but they may be multiple, especially in animals.

Macroscopic appearance of hard fibroma.—Hard fibroma is a nodular or lobular firm growth, variable in consistence, circumscribed, and well defined from the surrounding tissues. It is generally encapsulated, light in color, slow growing, and usually small in size, but it may reach enormous size in the body cavities. It is somewhat dry, cutting with tough resistance like a tendon, and is glistening in appearance on the cut surface.

Microscopic appearance of hard fibroma.—On microscopic examination the bundles of fibers are found to be coarse in texture, wavy in their course, frequently interwoven, crossed, and interlaced in a most complex manner, and form whorls around the scanty blood vessels. Between the bundles a fair number of spindle-shaped cells are present. These cells are rather inconspicuous owing to the small amount of cytoplasm. The presence of elastic fibers in fibromas, although doubted by some observers, can be found in the denser forms of fibroma in animals.

Structure of soft fibroma.—Soft fibroma, or fibroma molle, is soft in consistence, rich in cells, poor in fibrillar tissue, and is abundantly supplied with blood and lymph vessels.

Macroscopic appearance of soft fibroma.—The color of fibroma molle is gray or grayish red, in contrast to the glistening white color of the hard fibroma. The shape may be nodular, often lobulated, and not infrequently polypoid or pedunculated when growing from a mucous membrane.

Microscopic appearance of soft fibroma.—On microscopic appearance the connective-tissue bundles are seen to be more delicate and smaller in size and more loosely arranged than in hard fibromas. The cells are more numerous, possessing a considerable quantity of cytoplasm around the oval nuclei. They vary in shape and may be round, oval, spindle shaped, and irregular. Wandering cells, plasma cells, and leucocytes are often present.

Combinations.—Fibromas may frequently combine with other tumors, forming combinations in which the fibroma predominates, and the neoplasm is named by combining the two names, but naming the predominating tissue first, as in fibromyoma or in myofibroma. The more common combinations of fibroma with other tumors are fibromyoma, fibrolipoma, fibrochondroma, fibroosteoma, fibroangioma, fibroadenoma, fibropapilloma, etc.

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At times it is difficult to draw a sharp line between the hyperplasias of connective tissue resulting from chronic inflammation as in chronic mastitis, and true fibromata. Diffuse hyperplasias of the viscera, which at times are inflammatory, are generally considered by most authorities as cases of diffuse fibrosis.

Degeneration.—Serious infiltration and mucoid degeneration are often present in polypoid fibroids originating in the submucosa of the respiratory tract. Calcification and ossification have been reported but are rather rare.

Nature.—Clinically, fibromas are benign neoplasms which do not give metastasis to internal organs unless they are combined with malignant growths.

LIPOMA

Definition.—Lipoma or fatty neoplasm is made up of adipose tissue, which it closely resembles in appearance and structure. It may be found in all domestic animals and is rather common.

Seats.—Lipomas may grow wherever adipose tissue is normally present. The more common locations are the subcutaneous tissue in the region of the back, shoulders, breast, knees, inner surface of the thigh, the submucous tissue, and the subserous tissue of the mesentery, omentum, and peritoneal cavity.

The less frequent places to find lipomas are the liver, kidney, lung, mammary gland, ovary, and uterus.

Very rarely lipomas are found in the membrana nictitans in the horse and dog, also in the brain, arising from the blood vessels of either the pia mater or the dura mater.

Macroscopic appearance.—Lipomas are usually single but frequently may be multiple. They are slow growing, at times rather small, but have been known to reach enormous size. They are usually smooth, encapsulated, and can be readily shelled out of the capsule, being well circumscribed from the surrounding tissue. Their shape may be round or oval while they are small, when developed in the subcutaneous tissue, before they are subjected to pressure; but they become hemispherical or dome shaped when the pressure is from one side. When they become large the tension on the skin is sufficient to cause ulceration and even gangrene of the skin. Peritoneal lipomas in the omentum and intestines are often lobulated, especially in cattle, sheep, and hogs. The subserous intestinal lipomas in cattle may also be pedunculated. When the pedicle is stout and elastic a loop of the intestine may wind around it and cause strangulation in the intestine. A more unusual shape of lipoma is the diffuse form. Under this heading may be mentioned lipomatous elephantiasis. Lipomas may be firm or soft. If soft they are flabby. They are white or yellowish white in color, depending on the amount of connective tissue present and the composition of the fat. The fat of cattle, sheep, and hogs contains a higher percentage of stearin than of olein. In these animals the fat is whiter than in the horse. The fat of the horse contains more olein than stearin and is yellower and softer. The resistance varies according to the amount of connective tissue in the lipoma.

Microscopic appearance.—The individual fat cells and the lobules in lipomas are larger than those in normal adipose tissues. The

supporting connective tissue is coarser and contains fewer blood vessels.

Combinations.—Fibromatous change in lipomas is the most common. It is considered by many authorities to be more of a hypertrophy of the supporting fibrous connective tissue than a true combination with fibroma. Myxofibroma is not infrequent and may also be regarded as a fibrolipoma undergoing myxomatous change.

Degeneration.—Ulceration and necrosis in areas of isolated lobules may take place at times on the periphery of large lipomas. More rarely calcification is present, and then only in limited areas.

Nature.—Clinically, lipomas are benign neoplasms which give no metastases to internal organs.

XANTHOMA

In connection with lipomas there may be mentioned the xanthoma, a peculiar form of fatty neoplasm, which is a small, flat elevation, yellowish, found in the skin about the eye and eyelids, and more rarely about the internal organs in man. It is composed of modified fatty tissue resembling embryonal adipose tissue, with large vacuoles containing cholesterin esters (cholesterin and fatty acid clumps) and is supplemented by numerous round cells such as are found in cell infiltrations. Xanthoma has not been described from domestic animals.

MYXOMA

Definition.—Myxoma is a neoplasm composed of mucous tissue which is an embryonic connective tissue similar to that of the umbilical cord, or the jelly of Wharton, or the vitreous humor of the eye. As myxoma originates from a type of connective tissue from which fat develops in the embryo, the relation of myxoma to lipoma and fibroma is very intimate. These growths vary in size from that of a pea to the size of two fists.

Appearance.—Pure myxomas are soft, jellylike, translucent, encapsulated, grayish neoplasms, which are rather rare in their pure state. When their consistence is lacking in softness and gelatinous composition it would be more proper to consider such neoplasms as the myxomatous degeneration of a fibroma, lipoma, or sarcoma, instead of a myxoma. The most characteristic form of myxoma is the soft, grayish-colored, polyp-shaped mass commonly spoken of as nasal polypus. Myxoma may also appear as a hemispherical elevation projecting from a surface, or it may be lobulated, and occasionally it presents a diffuse mass without any definite limits, having no capsule.

Seats.—The mucous membrane of the nasal passages and the uterus of cattle are some of the common seats, also the serous membrane of the heart. Less common are the myxomas found in the mammary gland and those found in the course of the nerve trunks. Rarely myxomas are found in the marrow of bones and in the periosteum, also in the brain and spinal cord.

Structure.—On microscopic inspection myxoma consists of loosely scattered cells, some of which are spindle shaped, but most are star shaped with long processes that frequently anastomose with one another. These cells have a fair amount of cytoplasm and large, oval nuclei. Numerous fine, loose fibers, which are often gelatinous

in nature, are intermingled with the cells. Between the cells and fibers is the gelatinous, homogeneous, interstitial ground substance. A few blood vessels and lymph vessels are invariably present.

Combinations.—Myxoma is sometimes combined with fibroma, lipoma, and sarcoma, but most authorities are inclined to regard these combinations more as a process of mucous degeneration of the above-mentioned neoplasms rather than a combination with the myxoma.

Degeneration.—Myxomas frequently become edematous or undergo degeneration which is followed by the formation of a cyst.

Nature.—Clinically, myxomas are benign, nonmetastatic, slow-growing neoplasms. Their capsule is more delicate than in the fibroma of the lipoma and is often almost entirely absent when the myxoma assumes the lobulated form. At times, however, myxomas may grow rapidly, and the cell processes become absorbed, the interstitial substance is reduced in quantity, whereby the cells are closer together and the neoplasm develops a malignant tendency.

CHONDROMA

Definition.—Chondroma is a neoplasm composed of cartilage and a variable amount of fibrous connective tissue, which forms a capsule on the periphery and penetrates into the interior of the neoplasm.

Chondromas may be found in all domestic animals, especially in sheep, cattle, hogs, and horses, also rather commonly in dogs and domestic fowls.

Appearance.—Chondromas are nodular, lobulated, or rounded in shape, white or whitish gray, translucent when the hyaline cartilage predominates, and of a bluish-white tint on section. The color may be yellowish when elastic tissue predominates.

Seats.—Two distinct forms may be considered: (1) Chondroma proper or enchondroma, and (2) cartilaginous outgrowths or ecchondroma. The first, originating in noncartilaginous tissue, is the more usual form and is associated with the osseous system, starting from the periosteum and less frequently in the bone marrow. The sternum and ribs are frequently subject to injuries in domestic animals and are common seats of chondroma growing from the periosteum. The maxillary bone and the long bones are less frequently involved in the process. More rarely chondromas are found in the thyroid, parotid, and mammary glands, the testicle, and the ovary. In these localities chondromas must be the result of misplaced embryonic cell rests, congenital in origin, and are frequently combined with other neoplasms.

Ecchondromas or cartilaginous outgrowths originate from the perichondrium of the laryngeal, tracheal, and bronchial cartilages of the lung.

Structure.—Under the microscope chondromas usually resemble hyaline cartilage, less frequently elastic cartilage or fibrocartilage. The cells in chondromas are more irregular in shape and size, not only in different growths, but also in different parts of the same neoplasm. Several cells or groups of cells may be present in a lacuna and the capsule is generally absent. Some chondromas are very cellular, others are poor in cells. The smaller cells are always peripheral and the larger cells are central. Between the cells is the matrix, which is usually hyaline and homogenous or apparently

structureless, but may at times contain elastic or fibrous tissue. Chondromas, like normal cartilage, do not contain any blood vessels and derive their nutrition from the perichondrium or the capsule surrounding the periphery. For that reason they are subject to either retrogressive or progressive metamorphosis.

Combinations.—Chondroma frequently combines with sarcoma, myxoma, osteoma, adenoma, or lipoma, occurring in the mixed neoplasms found in the parotid gland, mammary gland, testicle, and ovaries. Of these combinations the chondromyxoma, chondrosarcoma, and osteochondroma are more frequent than the adenochondroma and chondrolipoma.

Degeneration.—Chondromas in domestic animals are very prone to undergo incomplete calcification or even ossification. The ground substance may be affected by mucoid degeneration with the production of softened foci and liquefaction resulting in the formation of cysts, which is less common in animals than in man.

Nature.—The ordinary chondromas are clinically benign neoplasms which give no metastasis and do not recur after removal. Exceptionally, however, metastases may be present even in the ordinary tumor and are always present in combinations of chondroma with sarcoma and in mixed neoplasms, when they become malignant, give metastasis, and recur after removal.

CHORDROMA

Resembling the structure of chondroma and myxoma, the chordroma may be mentioned; it is a rare, diminutive neoplasm of man which is about the size of a pea, occurring usually at the base of the skull in the vicinity of the spheno-occipital synchondrosis that corresponds to the upper end of the notochord, of which it is considered an embryonal remnant. It has also been described in the sacrum and coccyx. In structure it consists of cartilage cells, many of which are large and vesicular, and a homogeneous, jellylike, interstitial substance. It is usually benign when small, but more recently a number of cases have been reported in which it grew to a large size infiltrating the brain substance and becoming malignant.

This neoplasm has not been described in the domestic animals.

OSTEOMA

Definition.—Osteoma is a neoplasm composed of bone tissue. In the domestic animals there are a number of osseous deposits which result from injuries or inflammation of the periosteum that are osteoid conditions but are not true osteomas. The true osteomas are usually small and slow-growing neoplasms attached to the bony skeleton. They may occur, however, unattached to bones, as in the lung, testicle, parotid gland, mammary gland, ovary, and uterus.

Osteomatoid conditions, such as small protuberances projecting from the surface of the bone, the exostoses, osteophytes, splints, and spavin are the result of chronic inflammation and should not be considered as osteomas.

Appearance.—Osteomas may be of various shapes. Usually they are nodular, hard, at times lobulated, but always firmly or intimately attached to the surrounding tissue. According to the density of the caseous elements, three varieties may be distinguished: (1) Osteoma

eburneum, of ivorylike hardness and density; (2) osteoma spongiosum, resembling the structure of spongy bone; (3) osteoma medullosum, composed mostly of marrow, supported and reinforced by bone spicules.

Seats.—The tips of the horns in cattle are often the seat of osteomas. Injuries and inflammation to the damaged part may have contributed their share in the formation of horn neoplasms. Large and common osteomas may be found arising from the sphenoid, ethmoid, or the turbinate bones in cattle and horses. The mandible and inferior maxilla are other frequent places, as are any of the bones of the head, especially in the region of the orbits.

Structure.—Osteoma eburneum closely resembles compact bone. It is made up of bone lamellæ, lacunæ, and canaliculi, which are generally short and ill defined. Some of the lamellæ form in a concentric manner around the Haversian canals; these are the Haversian lamellæ. Others unite the Haversian systems; they are the interstitial or ground-bone lamellæ.

The arrangement of the lamellæ in osteoma is like that of normal bone—external or circumferential, Haversian or concentric, and interstitial or ground lamellæ. The Haversian canals are less regular and their course is at right angles to the axis of the bone. The larger canals may contain marrow. The periphery has a closely adherent capsule which is identical with the periosteum of bone.

Osteoma spongiosum has the structure of spongy bone, and the Haversian canals are expanded to form marrow spaces and loose interlacing meshwork of osseous structure, the interior of the spaces being occupied by cell structure identical with red marrow. The blood vessels are more numerous than in the preceding variety.

Osteoma medullosum is composed principally of marrow and has fewer bone spicules than the osteoma spongiosum. The capsule in the last two varieties is well developed.

Combinations.—Osteoma frequently combines with other neoplasms as osteofibroma, osteochondroma, and especially osteosarcoma.

Degeneration.—Secondary degenerative changes, softening, and necrosis are not infrequent in the spongy and medullary varieties.

Nature.—Osteoma is a benign neoplasm, nonmetastatic, and encapsulated. Though usually small, as in the dense variety, the spongy variety may reach the size of a football. Osteoma may be single but more often it is multiple. When in combination with sarcoma it becomes malignant and gives metastasis.

ODONTOMA

Odontoma is the name applied to excrescences on teeth. They are of bonelike hardness, congenital in origin, and composed of dentine, enamel, and pulp tissue. All these tissues are in variable proportion. Simple odontoma affects a single tooth and is met with in cows and horses. It usually surrounds the crown, or more rarely the root of a tooth. It is usually hard, rounded in shape, about the size of a walnut, but has been known to reach the size of an orange.

The mixed odontoma is soft, composed to a large extent of fibrous tissue, numerous blood vessels, odontoblasts, tooth-papilla structure, and rudimentary masses of dentine and enamel mixed in the interior and found also as a thin, peripheral crust. The mixed odontoma may

surround a single tooth, but more often involves a number of teeth. It may occur as a group of cysts completely surrounded by a fibrogelatinous dental sac and an alveolar bone capsule. It is sometimes described as odontosystoma.

Bland-Sutton (*3*) has given a most complete description of seven different varieties of odontomas in man; but, as such varieties are not recognized in the domestic animals, no further reference will be made here.

MYELOMA

Definition.—Myelomas are neoplasms which are formed from red bone marrow. They vary in color from grayish to yellow, but may be pink and often are deep red. Myelomas occur as primary multiple growths in the cancellated portion of the sternum, ribs, and skull, and according to some authorities less frequently in the long bones except in the tibia, where it is admitted to be not infrequent. They are benign and slow growing.

Structure.—The structure suggests a hyperplasia of the red marrow. During growth they induce active absorption of the bone and an invasion of the soft tissues. Microscopically these neoplasms consist of myelocytes, lymphocytes, erythrocytes, and a scanty amount of interstitial connective tissue. Often giant cells are present. The presence of giant cells was responsible for some pathologists' classifying the myelomas as myelosarcomas. They are frequently very vascular and rather liable to show hemorrhages. The naked-eye appearance and the microscopic appearance therefore suggest malignancy, though these neoplasms are invariably benign in nature and do not metastasize. There is a tendency of the hemorrhagic forms to become cystic.

MYOMA

Definition.—Myoma is a neoplasm composed of striated or nonstriated muscle fibers and a variable amount of connective tissue. According to the variety of muscle, myomas are divided into leiomyoma, composed of involuntary or nonstriated muscle, and rhabdomyoma, composed of voluntary or striated muscle. Of these two varieties leiomyoma is more common and occurs where involuntary muscle is normally present, as in the digestive tract, the reproductive organs, and the urinary system, whereas rhabdomyoma frequently occurs in places where voluntary muscle does not exist normally and is therefore considered to be of congenital origin.

Appearance.—Myomas are firm, pale, globular, rounded, nodular, or diffuse structures which more rarely become pedunculated. They vary in size from a pinhead to a man's head and even larger. They are so similar to fibromas, with which they frequently combine, that a differentiation can be made only by microscopic examination. This is especially true of myomas in the uterus. In this location they are often called fibroids until a microscopic examination proves them to be myomas.

Myomas are surrounded by a connective-tissue capsule. They are slow growing, sometimes single, but more often multiple.

Seats.—The most frequent seats are the muscle walls of the uterus and vagina in cows and hogs, and sometimes in dogs. The less

frequent locations are the esophagus, stomach, and intestines in horses and cows, the urinary bladder in dogs, and the serous membranes. The rarest place in domestic animals, but not in man, is the skin. Here myomas originate from the erector piliform muscles of the skin, from the ducts of the sweat glands, from the nipples, or from blood vessels.

Structure.—Microscopically, myoma consists of spindle-shaped cells with rod-shaped or cylindrical nuclei. The cells are arranged in compact bundles which interlace with one another at various angles. The individual cells are held together by a small quantity of cement substance which is collagenous in nature. At times myoglia fibrils have been seen lying alongside of the cells. It is very important to distinguish the spindle-shaped cells of involuntary muscle of leiomyoma from the spindle-shaped cells of soft fibroma and the spindle-shaped cells of spindle-cell sarcoma, as the last two varieties often enter into combination with the leiomyoma and it is not easy to distinguish them. The muscle cells of leiomyoma are usually long, slender and sharply outlined, terminating in a pointed extremity. Their nuclei are long, rod shaped, with rounded ends, and lie within the cell body. Sometimes the muscle cells, as in blood vessels, are short and plump.

The fibroblasts of the cellular fibroma, although spindle shaped, are shorter, and in those places where they form strands or bundles the very character of fibrous tissue is apparent. The principal distinction, however, lies in the fact that the nucleus of the cellular fibroma is short and oval and is peripherally situated. The small-sized neoplasms are much more likely to be pure myomas, while with the increase in size the fibromatous elements predominate in proportion to the diminution in the amount of involuntary muscle. It is for this reason that many of the uterine neoplasms which in reality are fibromyomas are commonly called fibroids. Leiomyoma may be distinguished from spindle-cell sarcoma by greater regularity in the direction of the cells, but particularly by the oblong rod-shaped outline of the nucleus, which is characteristic of leiomyoma.

Combinations.—Myomas frequently combine with other neoplasms, the most frequent combinations being fibromyomas, myxomyomas, myosarcomas, and adenomyomas.

Degeneration.—Calcification is the most common change. Myxomatous change may occur in myomas, which have a preponderance of fibrous connective tissue. Very rarely telangiectasis may be present in the peripheral parts of certain myomas, while the central part of the large neoplasms may be so poorly nourished that hyaline and later necrotic change may set in and result in cystlike softening.

Nature.—Myomas are slow growing, encapsulated, benign, nonmetastatic neoplasms. In combination with sarcoma they become malignant, produce metastases, and grow fairly rapidly.

RHABDOMYOMA

Description.—Rhabdomyoma is a rare neoplasm in both man and domestic animals. The characteristic tissue from which it derives its name is striated or voluntary muscle, which is always subordinate to other tissues, especially fibrous connective tissue and cells resem-

bling sarcoma. The greater part of the neoplasm may not contain any striated muscle fibers. Only here and there isolated fibers, or groups of striated fibers, may be present. Rhabdomyoma usually occurs in places where striated muscle is not normally present, except in the heart.

Seats.—The most common seat by far is the kidney, then the testicle, heart, vagina, uterus, bladder, and parotid gland. A case was reported found in the lung of a young sheep. The presence of this neoplasm in places where no voluntary muscle normally exists is an indication of congenital origin. In the kidney rhabdomyoma reaches the largest size, appearing as a rounded or irregular mass, which may lead to a total destruction of the organ. Rhabdomyomas of the testicle are not so large as those of the kidney and are less destructive. The rhabdomyomas of the heart are frequently pedunculated.

Structure.—On microscopic examination the striated fibers in rhabdomyomas are smaller than normal muscle fibers, more irregular, and often spindle shaped, or even club shaped. The sarcolemma is generally present and often droplets of glycogen can be demonstrated. The striation of the muscle fibers is faint and in places may be entirely absent. Fibrillar connective tissue and spindle-shaped, sarcomalike cells, some of which are suggestive of embryonal muscle cells, predominate.

Nature.—Rhabdomyomas are malignant in proportion to the amount of sarcomalike element which they contain. Adenomatous elements may be present, in which case the neoplasm is practically benign.

NEUROMA

Definition.—Neuromas are neoplasms composed of newly formed nerve tissue. The term is indiscriminately applied to any new formation occurring in the course of nerves. A distinction therefore should be made between the neoplasms consisting of nerve fibers, ganglion cells, or both combined, which are the true neuromas, and neoplasms without any increase in nerve fibers or ganglion cells. The latter are composed merely of a fibroconnective tissue enlargement or overgrowth on a nerve trunk, and are false neuromas, commonly called neurofibromas or fibroneuromas. The true neuromas are rather rare in man and almost unknown in domestic animals, whereas the false neuromas are comparatively common in man as well as in animals. Following neurectomy there are terminal thickenings on the nerve stumps, and although they are called amputation neuromas they are simply the regeneration process of the resected nerve trunk, but not neoplasms.

Appearance.—Neurofibromas develop as corded, cylindrical, fusiform, or even nodular thickening of nerve trunks. The perineurium undergoes a marked proliferation, forming a grayish structure which extends along many of the nerve funiculi in a nerve plexus and giving rise to an intertwining plexiform growth.

Seats.—Ostertag (*14*), Kitt (*11*), Morot (*13*), and others have observed these plexiform neurofibromas in the brachial plexus of cattle, and the dorsal, intercostal, and sternal nerves as nodular

thickenings. Thirteen hundred and fifteen such nodules in one old cow were recorded by Morot. Neurofibromas have also been reported in horses and pigs.

Among the rarer forms of neuromas and neurofibromas in man may be mentioned the painful subcutaneous tubercle, ganglion neuromas, and the multiple molluscum fibrosum, a nodular elevation of the skin.

GLIOMA

Definition.—Gliomas are neoplasms which grow from the cells of the neuroglia or glia, the supporting tissue of the central nervous system. Several authenticated cases have been recorded by Kitt (*11*) in dogs and also in other domestic animals. In man it is the most common neoplasm of the brain.

Appearance.—Glioma is usually a solitary neoplasm, rounded or oval, but difficult to distinguish from the normal brain. It is usually about the size of a cherry but may become as big as an apple. It is either soft or moderately firm and usually grayish white, but at times is dark red, when it appears sharply defined from the brain substance. In the last case it is traversed by numerous blood vessels and may contain hemorrhagic areas.

Seats.—Gliomas occur most frequently in the brain, less frequently in the spinal cord, and rather rarely in the retina. Gliomas of the brain and cord do not metastasize to other organs, but they may invade or disseminate in the tissue where they originally started. In their pure state gliomas are benign except for their situation; they may become dangerous by causing intercranial pressure or producing paralysis by pressure on a motor center, or may cause sudden death by hemorrhage. The retinal glioma is an extremely malignant and more rapidly growing neoplasm. Another rapidly growing glioma occurs in the adrenals, and is rarely found in the nervous system proper. The adrenal gliomas have a tendency to metastasize to the lymph glands and the liver. In the retroperitoneal region there is also a benign form of glioma originating from the sympathetic nervous system which from a predominance of large ganglion cells is called ganglioneuroma.

Structure.—Under the microscope neuroma consists mainly of small, round cells which are larger than ordinary glia cells, with prominent round or oval nuclei and numerous delicate branching processes. Some of the cells may possess a large amount of cytoplasm and several nuclei. The interstitial glia or neuroglia framework may consist of such delicate fibrils that the structure is as cellular in appearance as a sarcoma, and for that reason gliomas are often spoken of as the sarcomas of the brain. It must be borne in mind that the glia elements are of ectodermal and not entodermal origin. The gliomas starting in the retina are very cellular in structure. Some gliomas may have an abundance but never a predominance of neuroglia fibers, while the glioma of the sympathetic system has a considerable number of large ganglion cells, from which it receives the name ganglion-cell neuroma. In some gliomas groups of ependyma cells form rosettes around the blood vessels, resembling the tubules of adenoma. These neoplasms are called gliosarcomas by some pathologists.

Degeneration.—Degenerative changes are frequently found in the gliomas and lead to fatty degeneration, followed by softening, and often result in the formation of cysts.

ANGIOMA

Definition.—Angiomas are neoplasms composed of vascular tissue. If formed of blood vessels they are called "hemangiomas," when formed of lymph vessels they are called "lymphangiomas." They have a relatively small amount of supporting tissue. In either case there must be new formation or proliferation of the vessels. The distention alone of preexisting vessels, without proliferation, does not constitute angioma, any more than the alteration in the blood pressure of a local venous obstruction. Neither do capillary telangiectases, which can take place in local areas of the liver by a partial obstruction of a branch of the hepatic vein; nor do hemorrhoids, which are instances of compensatory dilatation of vessels, constitute angiomas.

Hemangiomas or angiomas proper are usually composed of proliferating and dilated vessels, arteries, veins, or capillaries and are classified as capillary angioma or angioma telangiectaticum. If the blood spaces are large, irregular, and intercommunicating they are designated as the cavernous type. Usually there may be gradations of these two types where the vascular channels are larger than capillaries but not large enough to be called venous spaces.

Seats.—In man there is found a superficial form of skin angioma that is rarely seen in domestic animals. This is probably due to the larger amount of pigment and the thickness of the skin in animals. However, the finding of this type of angioma at the root of the tail in dogs and horses has been reported. A comparatively common form of angioma, which is congenital, is the angioma simplex or the capillary form of angioma found in the skin of man about the face and known as birthmarks.

Structure.—Angiomas consist of capillaries with preformed, imperfect, thin-walled vessels resembling veins. The presence of these vessels conveys a bright-red color to the skin, but its surface is not raised. Rarely the walls of the vessels are thickened and tortuous in their course, superficially situated, forming palpitating groups of vessels in the scalp, which suggest in appearance a bunch of creeping earthworms. This form is described by some writers as angioma plexiform, angioma racemosum, or circoid aneurism.

Cavernous angioma.—Cavernous angioma consists of vascular channels which are dilated to the extent of large, communicating spaces lined with endothelial cells. The spaces are supported by interstitial connective tissue. These spaces are venous channels and suggest the structure of the corpus cavernosum. When situated in the skin they appear as dark red to almost bluish, extensive blotches that are commonly known as "port-wine stains," vascular nevi, or blue warts. Cavernous angiomas, like the angioma simplex or telangiectaticum, occur in the skin and also in internal organs, of which the liver is the most frequent seat in man. It is also very common in the liver of cattle and hogs, but may also be found in other domestic animals. Less frequently angioma is found in the kidney, spleen, intestine, bladder, muscles, bone marrow, brain, dura mater, and very rarely in the spinal cord.

LYMPHANGIOMA

Lymphangiomas are neoplasms consisting of dilated lymph vessels or lymph spaces. They are either acquired or more often congenital in man. In domestic animals they are unimportant and rarely found. Several cases of lymphangioma have been reported in the pleura, pericardium, and heart in horses and as superficial skin changes about the nipples in cats. It is often difficult to separate dilations of lymphatic channels due to obstruction from hyperplastic processes. The dilated lymph vessels usually preserve the original channels, as in lymphangioma simplex, or the number of the lymph vessels may be increased and their spaces enlarged, as in lymphangioma cavernosum; or the lymph spaces may form cystic dilations, as in the cystoid lymphangiomas.

Among the congenital lymphangiomas of man may be mentioned macroglosia, a congenital enlargement of the tongue, macrocheilia, the enlargement of the lips, and nevus lymphaticus of the skin.

Dilated lymph channels are accompanied by stasis of the lymph caused by the presence of a parasite, *Filaria sanguinis*, which produces a hyperplastic process in the skin that is known as elephantiasis or diffuse fibromatosis. This condition is sometimes found in horses and should not be taken for a neoplasm.

LYMPHOMA

Definition.—The name "lymphoma" designates a progressive proliferation of lymphadenoid tissue. The enlargement of lymph glands constitutes a debated subject in pathology. Formerly the name of lymphoma was used indiscriminately for all enlargements of lymphatic tissues independently of their cause.

Seats.—Lymphomas start in any of the lymphoid tissues, which are so widely distributed in the animal economy. They frequently have their genesis in the lymph follicles or nodes found in mucous membranes, and in the compound lymphadenoid structures, as the lymph glands. They are found in the course of lymph vessels, or in the spleen, the red bone marrow, and thymus glands. These lymphoid tissues are regarded as the parent source of leucocytes and lymphocytes, and are therefore affected by disturbances of the circulation and blood disorders. Lymphatic tissue reacts most readily to infective agents in all diseases of a septic and infectious nature. Any irritant that is responsible for an acute or chronic disease produces enlargement of the lymphadenoid tissues.

Conditions resembling lymphoma.—Inflammatory enlargements of the lymphoid tissues are not true neoplasms. It is often very difficult to differentiate between them.

Acute inflammation of the lymph glands which is manifested in the hyperplastic or in the exudative form is common in man and very common in domestic animals. The chronic form is as common in man as in the lower animals. The lesions may occur in a single node, but are more frequently found in several nodes of the same group, or in groups situated in different parts of the body. Tuberculous lymphadenitis is the most frequent of these lymph-gland enlargements in domestic animals, especially in cattle and hogs. The lymph glands are enlarged, often contain hemorrhagic areas, may

show caseation and calcification in the later stages, and upon microscopic examination show the presence of tubercle bacilli. In cattle there may be a tendency to excessive hyperplasia of the lymphoid structures without the presence of recognizable tubercle bacilli. The name of paratuberculous lymphadenitis has been applied to this condition by some observers.

Enlargements of lymph glands in hog cholera should not be overlooked, but the lesions in the skin, kidneys, and digestive tract make possible a differentiation of these gland enlargements from tuberculous lymphadenitis.

Simple or typical lymphoma, described by some writers as hyperplasia of the lymph nodes, constitutes another form of lymph-gland enlargement, the etiology of which is still in doubt. The thymus gland in calves, hogs, and dogs may be greatly enlarged and become confluent. Either a single gland or a group may be affected, and the enlarged gland may remain for a considerable time without any change. The capsule of the gland becomes thickened. On microscopic examination the general anatomical division of a normal lymphoid node is preserved. The germinal centers are often increased in size and show hyperplasia. The lymphocytes, although morphologically normal, are less densely arranged between the stouter connective-tissue trabeculæ.

LEUKEMIC LYMPHOMA

Leukemic lymphomas may be acute or chronic in character. The acute forms occur at a younger age, whereas the chronic form is invariably found later in life. Microscopically, real lymphatoid overgrowth is shown by the overdevelopment of lymphocytes, reticulum, and sinuses. An excess of lymphocytes appears in the circulating blood. This latter condition facilitates the diagnosis of leukemic lymphoma from the other forms of lymphoma.

PSEUDOLEUKEMIC LYMPHOMA

Pseudoleukemic lymphoma or pseudoleukemia in animals, or Hodgkin's disease in man, is another type of lymphatic hyperplasia, with diffuse widespread enlargement of the lymph nodes but without the increase of leucocytes in the circulating blood. Large numbers of lymph nodes may be affected in various regions. The spleen is invariably involved, but the bone marrow is not altered, as a rule. Later in the disease the liver undergoes enlargement and the kidney may also become affected. Histologically the enlarged lymph gland shows no infiltration. The hyperplasia is due essentially to the overgrowth of the connective-tissue reticulum, marked prominence of the endothelial cells, and an actual reduction of the lymphocytes and the cells of the germ centers. There may be an abundance of eosinophiles. Increase of connective tissue in the capsule, trabeculæ, and reticulum of the pulp becomes the marked feature, particularly in the spleen.

SARCOMA

Definition.—Sarcomas are richly cellular, malignant neoplasms of connective-tissue origin. The cells are imperfectly differentiated or embryonic in type, with a scanty amount of intercellular substance

between them. Sarcomas occur frequently in man and in all domestic animals.

Appearance.—Sarcomas are variable in size, shape, color, and consistence. They may be circumscribed or nodular, but more frequently they are diffuse and infiltrate the surrounding tissue. When growing near the surface they may finally protrude from the surface as red, granular masses resembling exuberant granulation tissue of healing wounds. This appearance, resembling flesh, led the older observers to name such neoplasms sarcomas, from the Greek word "sarko," fleshlike. The consistence of sarcomas depends partly on the shape of the cells and partly on the presence of the intercellular substance. This is particularly true when fibrous tissue, cartilage, and bone enter into combination with the neoplasm. The compactness or closeness of the cell arrangement and the vascularity influence not only the softness and the density but have a direct bearing on the color found in different types of sarcomas, which will be described later. The dark-brown to black color of certain sarcomas is due to the presence of melanin, which is a pigment derived from cell metabolism. With the exception of the giant-cell sarcomas, which are partly encapsulated, primary sarcomas, as a rule, are not encapsulated. Secondary sarcomas are more circumscribed and frequently show at least an attempt to form a capsule around the secondary nodule.

Seats.—Sarcomas always start from preexisting connective tissue of the body. The skin and the subcutaneous tissue, also the intermuscular tissue, fascias, the sheaths of tendons, the periosteum of bones, the perichondrium of cartilage, and the bone marrow, are among the most common seats for their growth. Less frequently sarcomas are found in the subcutaneous connective tissue of the respiratory system and of the reproductive and urinary organs, also in the serous membranes of the pleural and peritoneal cavities, in the membranes and the nerve tissue proper of the brain and cord or in the supporting tissue, or in the adventitia of the blood vessels of the choroid plexus. In the liver, pancreas, lung, and heart, they may appear, but usually by metastasis.

Structure.—Sarcomas retain the cellular structure and undifferentiated type throughout their growth. The cells of sarcomas vary in shape, being round, spindle shaped, or polymorphous in form. There is usually a scanty amount of intercellular substance. Their nuclei are large, leaving but little cytoplasm around the periphery. In rapidly growing forms the nuclei are hyperchromatic, stain well with nuclear dyes, and appear granulated or vacuolated, but they stain poorly after degenerative changes have set in. With proper fixation karyokinetic figures may be seen in spite of the small size of the cells. In most sarcomas the intercellular substance is scarcely appreciable, but it may become sufficiently pronounced in some varieties to form well-defined bands of the stroma, which separate the cells into groups or columns, forming an alveolar appearance.

Sarcomas have a different blood supply from other neoplasms. The walls of their blood vessels are imperfectly formed and consist of scarcely more than a single layer of endothelial cells, and in some instances of mere clefts in the sarcomatous tissue through which the blood flows. The thin walls in sarcomas favor frequent hemorrhages and the detachment of sarcoma cells into the blood current to form

finally metastatic deposits. Sarcomas have no lymphatics or nerves, according to most authorities. This is the reason that metastases of sarcomas take place by the blood vessels rather than the lymph channels, except in lymphosarcoma.

Combinations.—Sarcomas may combine with many other neoplasms. The combination with fibromas is very common in all domestic animals. All gradations of fibrous tissue, from a mere trace to a decided excess, may take place. The development of fibrous tissue in a sarcoma has a tendency to make the sarcoma less malignant. In naming these combinations, the name of sarcoma is invariably used last, as in fibrosarcoma, chondrosarcoma, osteosarcoma, myxosarcoma, etc.

Degeneration.—Nearly every form of degeneration may affect sarcomas, especially the more rapidly growing varieties. Fatty degeneration, liquefaction, necrosis leading to the formation of cysts, and ulceration are more common than mucoid degeneration, hyaline degeneration, caseation pigmentation, or amyloid degeneration. It is also customary to speak of angiomatous change, cavernous change, telangiectatic change, fibrous change, etc. These terms denote no special change of degeneration, but are used simply to express the combination of the sarcoma with the other tissue by a different name. Sarcomatosis is a condition characterized by the formation of multiple sarcoma deposits in the skin or in the internal organs. Sarcomatosis in fowls is somewhat common.

SPINDLE-CELL SARCOMA

Spindle-cell sarcoma is a very common neoplasm in man and in the domestic animals. The neoplasms vary in size, usually growing slowly as a single mass, but may be multiple when they grow more rapidly. The cells are either small or large, spindle shaped, elongated, tapering toward the ends. The cells of the small spindle-cell sarcoma are from 10 to 20 microns in length, or approximately one and one-fourth to three times as long as the diameter of a red blood corpuscle (human). The cells resemble fibroblasts. Dense connective tissue in the skin, the fascias, perichondrium, and periosteum are some of the places in which spindle-cell sarcomas most frequently grow. These neoplasms may be very cellular, or may have so much fibrous tissue as to simulate a fibrosarcoma. Such neoplasms are frequently called intermediate types.

The cells in the small spindle-cell sarcoma are usually uniform in size, compactly arranged in interlacing bundles or fasciculi, with very little intercellular substance between them. The nuclei are oblong, not so long as the nuclei of involuntary muscle, but longer than those in fibroblasts. In sections the interlacing bundles of spindle cells are cut at various angles to the axis of the cells, giving the impression that spindle-shaped cells, oval cells, and round cells are intermingled. It is important not to consider this appearance as a mixed type of spindle-cell and round-cell variety of sarcoma. The cells take the nuclear stains well unless degenerative changes are present. These neoplasms are grayish white in color, moderately firm, and not very vascular. They grow very slowly, but may become very large. Small spindle-cell sarcomas, as a rule, are less malignant and less prone to give metastasis than other varieties of

sarcoma which are softer and more vascular. The less malignant spindle-cell fibrosarcoma may be encapsulated, and when subcutaneously situated and multiple they are sometimes called "recurrent fibroids."

The large spindle-cell sarcoma differs from the small spindle-cell sarcoma in the size of the cells, which range from 50 to 80 microns, or from four to six times the size of the small spindle-cell variety. The cells are less uniform in size, and often show all gradations in the size of the cells. The nuclei are large, usually oval, sometimes granular, and often vascular. The bundles of cells are less interlacing and are more nearly parallel in disposition. Large spindle-cell sarcomas are not so compact, owing to a large amount of intercellular substance. Large spindle-cell sarcomas occur less frequently than the small spindle-cell variety.

ROUND-CELL SARCOMA

Round-cell sarcomas are found as commonly in domestic animals as in man. They are the most common variety of sarcoma in man, and according to some observers are even more frequent in domestic animals than spindle-cell sarcomas. The cells may be small or large.

Small round-cell sarcomas are the most malignant form of sarcoma. Their malignancy is due to infiltration and destructive properties, as well as the readiness with which they form metastatic deposits in internal organs. Small round-cell sarcomas are soft to the touch, pinkish-red or fleshlike in color, very vascular, and often so hemorrhagic as to justify the name of "telangiectatic" or "bleeding sarcoma." The cells of the small round-cell sarcoma are about the size of lymphocytes, and their nuclei occupy practically the entire cell, leaving very little cytoplasm around the granular, well-staining nuclei. There is very little intercellular substance between the small globular cells, which enables the loosely clumped cells to metastasize more easily than the overlapping and compactly arranged cells of the spindle-cell sarcoma. Small round-cell sarcomas may occur in any part of the body wherever connective tissue exists. They grow rapidly, infiltrate the surrounding tissues, and recur after removal. Because of their rich blood supply and the thinness of the walls of their vessels, they give metastatic deposits to all internal organs, but especially to the lung, liver, spleen, and kidney.

The large, round-cell sarcoma consists of cells that are often larger than the mononuclear leucocytes. The cells are more variable in size and less regular in shape than the cells of the small, round-cell variety. The nuclei are relatively smaller, with a generous quantity of cytoplasm around them, which gives them the appearance of cells of the epithelial type. The cells stain less deeply than in the small, round-cell variety, and appear more loosely arranged, on account of the abundance of the interstitial substance. Large, round-cell sarcoma occurs less frequently than the small, round-cell sarcoma, and is not so malignant. Several cases in the mammary gland, the ovary, and the testicle have been described, but the neoplasm may be found in other locations.

LYMPHOSARCOMA

Lymphosarcoma or malignant lymphoma is a variety of round-cell sarcoma which produces more cell reaction than a simple hyperplasia of a lymphatic structure. The principal characteristic of lymphosarcoma is that it infiltrates and perforates rather than metastasizes. These neoplasms are often found in the mediastinum and may involve any structure of the thoracic cavity. They grow rapidly, following the connective tissue of the mediastinum, and envelop the trachea and bronchi, following the interlobular connective tissue to the root of the lung. They may also extend along the aorta and larger vessels, invade the pericardium, and infiltrate the heart muscle. The infiltration may also extend along the esophagus, or along the course of the vagi or the phrenic nerves, as well as the sheaths of muscles of the diaphragm.

Lymphosarcoma in domestic animals occurs also in the abdominal cavity, producing marked thickening of the intestinal walls and the stomach. It is also frequent in the kidney, spleen, liver, and reproductive organs.

Microscopically lymphosarcoma consists of small, round cells identical in appearance with lymphocytes. The cells are fairly uniform in size and have a large nucleus slightly displaced to one side, leaving very little cytoplasm around the periphery and staining well with nuclear dyes.

Although the infiltrating property of lymphosarcoma follows the course of lymph vessels which is not the course of ordinary sarcoma, the infiltration from one lymph follicle to another follows, forming finally a fused mass, but does not become generalized as in leukemia. Such extensive local invasion by continuity of structure is referred to by some writers as lymphosarcomatosis. Metastasis by the blood vessels is very uncommon, and secondary deposits in other organs are rarely found.

ALVEOLAR SARCOMA

Alveolar sarcoma is not a separate variety of sarcoma so far as the appearance of the cells is concerned. Alveolar sarcomas are usually a subvariety of round-cell sarcoma, but may be also of the spindle-cell type, with the cells varying in size. It is probably more common in domestic animals than in man and is considered very malignant. The chief characteristic of alveolar sarcoma is the arrangement of cells in groups or nests simulating somewhat the lobules of a gland. These groups or islands of cells are separated from one another by bands or septæ of interstitial connective tissue. In rare instances the alveolar effect may be produced by an arrangement of spindle-shaped sarcomatous cells, but in the type most frequently encountered the alveoli are rendered more prominent by the connective-tissue trabeculæ separating the groups of cells, and this form is much coarser than the lymphadenoid reticulum found in the lymphosarcoma. The connective-tissue trabeculæ support the blood vessels, which may be very abundant. Alveolar sarcoma is highly malignant and grows where any sarcomas are found, but shows marked preference for the skin and serous membranes, notably the pleura and peritoneum. Alveolar large round-cell sarcoma may be mistaken for carcinoma if the character of the cells is not taken into consideration.

GIANT-CELL OR MYELOID SARCOMA

Giant-cell sarcomas are neoplasms characterized by the presence of multinuclear or giant cells, which are identical with myeloplaxes of bone marrow and are intermingled usually with the cells of spindle-cell sarcoma and sometimes with the cells of round-cell sarcoma. Giant-cell sarcoma, unlike other forms of sarcoma, is encapsulated, practically nonmalignant and not known to metastasize or to recur after removal. The giant cells of sarcoma are irregularly jagged in outline, often large, and may be from 10 to 30 times the size of leucocytes. They often have vacuoles and fat drops. The nuclei may be few in number or very numerous, since as many as 100 have been observed in a single giant cell. The nuclei in giant-cell sarcomas are scattered in the interior and all through the cytoplasms of the cell, and not at the periphery, as is the case in the degenerative type of giant cells found in tuberculosis or around foreign bodies. Giant-cell sarcoma has an extensive supply of capillary vessels from which blood extravasations may often take place. These extravasations give the neoplasm a brownish-red color. Giant-cell sarcoma is moderately firm, slow of development, and often even hard to the touch. In those starting from the bone marrow the hemorrhagic condition may be so abundant as to be mistaken for blood clots resembling currant jelly. Besides the ordinary type of giant-cell sarcoma originating from the periosteum of the jaw or the long bones, there is one variety that occurs in the gum and is known clinically as epulis. It is not uncommon in man, but is rarely found in domestic animals.

OSTEOSARCOMA

Osteosarcoma is sarcoma containing osseous tissue. During the early stages of its growth spindle-shaped sarcoma cells are intermingled with a variable quantity of immature bone and often with a few giant cells. Osteosarcoma is rapid in growth and malignant in nature. It is not uncommon in domestic animals especially in the maxillary bones. The neoplasm infiltrates into the epiphyses of long bones and extends also into the shaft of the bone, replacing the bone structure by imperfect osseous material. During the growth absorption of the bone from the periphery takes place. The tissue absorbed is replaced by an osteoplastic process, which must have been the initial condition responsible for the growth of the neoplasm. Different portions of the growth show microscopically various cells, such as sarcomatous spindle cells intermingled with cartilage cells, imperfect bone lamellæ, and atypical bone cells without branching, which indicate rudimentary bone formation.

Some forms of sarcoma of periosteal origin become intensely malignant. This type has a strong tendency toward calcification but not for true ossification. Metastases to serous membranes and the lung are not common. Some writers describe this type by the name of osteoid sarcoma.

MELANOTIC SARCOMA

Melanotic sarcoma is a pigmented, malignant neoplasm. The names "melanoma" and "melanosarcoma" are synonymous. These neoplasms are common in man but even more frequent in domestic

animals, especially in gray and light-haired horses. The most frequent places to find melanotic sarcomas are the skin and the choroid coat of the eye, where pigment normally exists. The skin at the root of the tail and the external genitals in horses are especially common seats, and the neoplasms occur less frequently in the adrenal glands and in the meninges of the brain. As secondary metastatic deposits melanotic sarcomas may be found in every organ, especially in the liver.

The dark color of melanotic sarcoma is due to the presence of melanin, a brown or black pigment elaborated by the connective cells as the result of metabolism. It was formerly supposed that melanin was of hematogenous origin, but chemical analysis has proved the absence of iron in melanin, whereas hematogenous pigments contain iron. Melanin consists of brownish-black granules found in the cells as well as between the cells. There may be present also a certain amount of diffuse melanin. The granules, which are variable in size, may be sparsely or densely distributed not only in different neoplasms but also in different parts of the same neoplasms. Any variety of sarcoma may become pigmented, especially the alveolar sarcomas.

The consistence varies with the shape of the cells and the amount of vascularity. The spindle-cell type is usually harder to the touch and generally less pigmented than the round-cell variety, which is not only softer but may be very vascular and almost black in color.

Melanotic sarcoma originating in the choroid coat of the eye is common in man and is very malignant, but is seldom found in domestic animals, and when found in them the liver is always involved.

COMBINATIONS OF SARCOMAS

The combinations, intermediate or mixed types, of sarcoma comprise all the atypical neoplasms in which sarcoma combines with benign connective tissue or with epithelial growths and converts them into malignant neoplasms. The most common forms of these mixed types are fibrosarcoma, chondrosarcoma, osteosarcoma, osteochondrosarcoma, myxosarcoma, liposarcoma, neurosarcoma, angiosarcoma, lymphangiosarcoma, gliosarcoma, rhabdomyosarcoma, and adenosarcoma. In all these neoplasms the original tissue indicates so plainly the type of the tissue that a variable amount of sarcoma cells does not prevent recognition by microscopic examination. A detailed description of these neoplasms would be only a repetition of the previously described structures.

ENDOTHELIOMA

Definition.—Endotheliomas are neoplasms which are composed of connective-tissue cells that have originated from the endothelial surface or lining of blood vessels or lymph vessels. When the new growth arises from serous membranes, such as dura mater, pia mater, peritoneum, pleura, or tunica vaginalis the name of mesothelioma is used by some writers. When arising from the endothelium of the perivascular lymphatics and the adventitia of blood vessels, it is known as perithelioma.

Nature and structure.—In origin and malignancy endotheliomas resemble sarcomas, but are less malignant and not so metastatic. In

structure and cell grouping they may resemble carcinoma very closely. Endotheliomas are rich in cells which are arranged in clusters or nests that suggest the acini of glands; hence these neoplasms are sometimes spoken of as endothelial cancers. This arrangement bears also close resemblance to alveolar sarcoma. The endothelial cells in the acini are often cylindrical in shape, forming cords or hollow tubes. The cylindrical cords may undergo hyaline degeneration and appear as homogeneous or hyaline masses, when the neoplasms are called cylindroma. Some endotheliomas originating in the dura mater or the pia mater may have a scanty stroma and numerous cell nests, in the interior of some of which globular clusters of lime salts are deposited. These deposits when found in the brain are known as psammoma or brain sand. Endotheliomas originating from the choroid plexus always contain a considerable amount of cholesterin in deposits and are therefore called "cholesteatomas."

Endotheliomas are rather slow-growing neoplasms and are only slightly malignant, hardly ever giving metastasis. They are not common in man or in animals, though several cases of endothelioma and psammoma from the spinal dura mater, the choroid plexus, and the anterior part of the brain have been reported in cattle. Cholesteatoma in the ventricles of the brain in horses has been described by several pathologists. Endotheliomas on serous surfaces are by no means rare in domestic animals.

EPITHELIAL NEOPLASMS

A brief consideration of the normal relation or grouping of epithelium in the adjacent structures aids in a proper understanding of epithelial neoplasms. Epithelium in the animal economy depends on connective tissue for support, as in the skin and in all mucous membranes, or for the grouping, as in the formation of glands (secretory) or in the compound glandular organs (liver, kidney, etc.). In other words, wherever epithelium is present it is intimately related with connective tissue, which participates during the growth of the neoplasms.

PAPILLOMA

Definition.—Papillomas are benign fibroepithelial neoplasms resulting as outgrowths from surfaces covered by epithelium. The neoplasm originating from a surface covered by stratified squamous epithelium is called hard papilloma, whereas the neoplasm starting from a mucous membrane lined by columnar epithelium is known as soft papilloma.

In its simplest form papilloma constitutes the common wart, which is simply a conical or rounded elevation of the derm covered by the epiderm, a thick, stratified layer of epithelium. Warts usually occur singly but may be multiple. Usually they are not painful, but when irritated they may ulcerate and bleed. They have been known to appear suddenly and sometimes disappear spontaneously. When persistent they may become large and may be readily mistaken for malignant growths. The connective-tissue elevation or core may become expanded at the apex and have secondary plications be-

tween which the epithelium sinks in, leaving an uneven surface not unlike the outside of a mulberry. At times the elevation of the core branches out, forming secondary plications, when the neoplasm assumes a grapelike or cauliflower formation. When the elevations are long and narrow the papilloma is known as villous papilloma. The weight of a downward-growing papilloma may stretch the core and form a pedunculated growth.

Seats.—Papillomas occur in the shape of warts, grapelike or cauliflowerlike clumps, or as pedunculated growths, common in man and domestic animals. The skin about the head and neck and also the udders of cows and about the legs of horses are common places. Such superficially located papillomas are readily exposed to traumatism, which renders them susceptible to infections, resulting in ill-smelling discharges. Frequently papillomas are found on mucous surfaces including the lips, mouth, tongue, larynx, esophagus, stomach, intestines, kidney, bladder, and endometrium, and rarest of all on the choroid plexus in the cerebral ventricles.

Structure.—On microscopic examination papillomas vary according to their shape, complexity of structure, and location. In the hard papilloma there is a connective-tissue stalk or core composed of fibrous-tissue bundles which are interlaced and contain a fair number of cells and a moderate amount of blood vessels. Stratified, squamous epithelium covers the stalk. The outermost cells are usually keratoid or horny. Papillomas growing on mucous membranes lined by columnar epithelium are softer on account of the more loosely arranged bundles, which are also fewer in number. The villous soft papillomas are found in the larynx, urinary bladder, and mucous surface of the esophagus, as well as in the kidney, ovary, and uterus. Unlike other benign neoplasms, papillomas are not encapsulated, because of their outward growth from surfaces. Serous degeneration or dropsical conditions are frequently present in the polypoid type of papilloma. Mucous or myxomatous degeneration is not infrequent in this type. Suppuration and ulceration are sometimes present.

ADENOMA

Definition.—Adenomas are usually benign epithelial neoplasms resembling the structure of a tubular or alveolar gland. They are usually single, slow-growing neoplasms, differing in shape in their attempts to reproduce the many types of glands from which they have originated.

Structure.—Adenomas, like their ancestors the glands, consist of epithelium, which corresponds to the parenchyma or functional part of the secreting gland, and the stroma forming the interstitial supporting tissue.

As there are many varieties of glands, such as the sweat and sebaceous glands of the skin, the uterine, mammary, and salivary glands, the liver, renal, and seminal glands, so there may be many kinds of adenoma differing in the shape and size of the acini and in the character of the lining cells, which may be shorter or longer than those from which they originated. In the earlier stages adenomas resemble glandular hypertrophies so closely that it is difficult to distinguish them from each other. With the growth of the neoplasm there is an increase in the complexity of structure resulting

from a process of budding of the preexisting tubules or saccules of the gland. Adenomas have no ducts, and any secretion that may be formed in the neoplasm remains in the acini, distending the alveoli, and forming cystlike dilatations. The neoplasm then is known as cyst adenoma. The retained secretion is of a degenerative character. In simple adenomas the epithelium rests on the basement membrane, as in a normal gland.

Destructive adenoma.—When the cell proliferation is so active that the epithelium has been desquamated, the neoplasm assumes a malignant tendency and is known as destructive adenoma, often found in uterine neoplasms, or as adenocarcinoma, which is frequently present in mammary and rectal neoplasms.

CARCINOMA

Definition.—Carcinoma or cancer is the type of a malignant epithelial neoplasm. The name "cancer" is universally used by the laity to designate a dreadful affliction in man and a hopeless condition in animals. This conclusion is derived from the fact that the number of deaths in man annually amounts to tens of thousands. No other neoplasm has received from scientists more attention, study, painstaking investigation, and special research to ascertain the true cause, the mode of propagation and spreading, and means of eradication and control.

Carcinomalike adenomas are epithelial neoplasms of glandular origin. Although the individual gland compartments in adenoma are tubular or alveolar in structure, with the acini lined by a single layer of cells and a lumen in the center of the acini, the epithelial cells of carcinoma are heaped up in irregular clumps, nests, or cylinders, which are continuous with one another. These clusters of epithelial cells penetrate the surrounding tissues by budding or by an extension of branching processes that have been compared to the roots of a tree or the legs of a crab. From this resemblance the name "cancer" originated.

The epithelial cells in cancers are the most conspicuous structures. The cells are in different stages of development and vary greatly in shape and size. Therefore, the statement sometimes found in print that "a typical cancer cell," found in a certain preparation or present in a certain neoplasm is diagnostic of cancer, is an erroneous and misleading impression. It is not the size, shape, structure, or variety of a cell that determines whether it is a cancer cell, but the relation of the parenchyma to the stroma that determines whether the epithelial cell and fibrous-tissue combination should be called carcinoma, adenoma, or papilloma.

A single cell isolated from a cancer can not be told with certainty from a normal epithelial cell. The epithelium in the cancer is the more conspicuous or basic structure, but the interstitial tissue, which may be either scanty or excessive, is of great importance in the development of cancers. According to Ribbert, (*17*) "cancers always start from chronically inflamed tissue."

Chronic inflammation of connective tissue brings about cell proliferation. The accumulated connective-tissue cells multiply and separate the epithelial cells by destroying the intercellular cement. The liberated epithelial cells then begin to multiply, acting collectively as

a foreign body, and as such attract leucocytes by their positive chemotactic property. The leucocytes are deposited around this area of multiplying epithelium. The epithelial multiplication continues to the extent of forming buds or roots which penetrate the newly formed hyperplasia constituting the stroma. The penetration takes place in the direction of the least resistance, which is along the course of the lymph vessels, and these therefore become the principal avenue for the extension of the cancer roots as well as the leading channels for the transmission of secondary cancer deposits.

The lymph glands that are interposed in the course of the lymph vessels act as temporary detention places or sieves for the retention of any particles which may be carried in the lymphatic stream. This is the reason that secondary carcinomatous deposits are transmitted by the lymph vessels and are generally multiple and numerous.

Appearance.—Carcinomas differ considerably in various parts of the body and may grow on free surfaces, where they are known as epitheliomas, or in the interior of organs, where when soft they are known as medullary cancers. Epitheliomas that start from the Malpighian layer of the skin and are composed of flat epithelial cells are known as squamous epitheliomas. The epitheliomas starting from mucous membranes lined by cylindrical cells are called cylindrical or columnar epitheliomas. The medullary cancers usually have an abundance of parenchyma and a scanty amount of stroma; when they are soft they are known as encephaloid or soft cancers. A preponderance of the supporting stroma conveys rigidity or hardness to the touch, and the carcinoma is known as scirrhous or hard cancer.

SQUAMOUS EPITHELIOMA

Definition.—Squamous epitheliomas are malignant epithelial carcinomas occurring in the skin and mucous membranes lined with stratified squamous epithelium. Epitheliomas are common in man and are even more frequent in domestic animals. The malignancy of epitheliomas is expressed by proliferation of the epithelial cells, the subsequent infiltration and destruction of the affected tissue leading to inflammation, suppuration, and ulceration.

Appearance.—Squamous epitheliomas differ somewhat in appearance, depending on the location and the structure of the affected part. When in the skin they appear as nodular elevations which are very prone to ulcerate. In the beginning the elevation hardly rises above the surface, but in the later stages epithelioma often assumes a dendritic shape. It then resembles a papilloma, differing, however, from the latter by its growth, which is only outward in the papilloma but both inward and outward in the squamous epithelioma.

Seats.—Squamous epithelioma is often found at the junction of the skin with a mucous membrane. This is the vulnerable point, beyond which the cornification of the skin does not extend into the mucous membrane, as at the conjunctival margin of the external auditory meatus, the external nares, lips, and muzzle. Less frequently it is found in the larynx, tongue, esophagus, cervix uteri, vagina (which is very often affected in women but seldom in animals), the penis in horses and dogs and also around the anus. Squamous epithelioma is rarely found in the bladder, scrotum, and pelvis of the kidney.

Structure.—Microscopic sections of squamous epithelioma show a perverted state of epithelial hyperplasia. In neoplasms from the skin the epithelium of the stratum Malpighii proliferates, forming cylindrical cords which extend inward and penetrate and invade the underlying connective tissue. These branching cords, though extending in different directions, are continuous with one another in sections and may show the epithelium in cylindrical groups or nests. The outer cells of these cords, which are in contact with the stroma, are cuboid or cylindrical, resembling the cells of the stratum germinativum. The cells in the interior of the cords are polyhedral, often larger in size than the cells found normally in the skin and resembling prickle cells. The inner cells, which are the oldest, are flattened, cornified, and homogeneous in appearance. They form concentric or lamellar groups that are known as "pearly bodies," which constitute the definite characteristic of squamous epithelioma in sections.

In man a special form of squamous epithelioma of the face about the eyes and nose has been described by some pathologists under the name of "basocellular cancer." This neoplasm is almost benign and shows no tendency to infiltrate the surrounding tissues. This form of epitheliomas has not been described in domestic animals.

The epithelial cords of squamous epithelium are separated by a variable amount of interstitial connective-tissue stroma. The stroma may be abundant or scanty, and is the tissue which contains the blood vessels and lymphatics. The stroma may consist of loose fibrous tissue or may be composed of tissue rich in cells. When ulceration affects the epithelial portion, the stroma becomes the seat of inflammatory cell infiltration.

CYLINDRICAL EPITHELIOMA

Definition.—Cylindrical epithelioma is a form of carcinoma which originates on surfaces lined by columnar epithelium or from glands of the columnar-cell variety.

Seats.—Cylindrical epitheliomas are found most frequently in the mucous membrane of the gastrointestinal tract and of the uterus, at the pyloric end of the stomach, at the ileocecal valve, and in the rectum, at the junction of the columnar epithelium with the squamous epithelium. The location last mentioned is considered the typical seat for the occurrence of cylindrical epithelioma. Less frequently is this neoplasm found in the mammary gland, the respiratory tract, kidney, and liver.

Nature and structure.—Cylindrical epitheliomas are soft to the touch, grow rapidly, are often papillary, and frequently ulcerate in the interior. They readily undergo degeneration, especially mucoid change, which makes them more malignant. On microscopic examination cylindrical epithelioma is seen to consist of columns resembling tubular glands. A lumen may be present between the rows of cells. When the columnar cells proliferate the tubular structure may consist of several rows of cells, the outer row retaining the columnar shape while the inner cells may be irregular, but the cylindrical epithelioma retains the tubular shape. When the lumen becomes distended the appearance is not unlike that of an adenoma.

The stroma of the cylindrical epithelioma is more loosely arranged and is more cellular than the stroma of squamous epithelioma. The looseness is due to the anatomical differences in the structure of the submucosa in which cylindrical epithelioma develops, from the denser and more compact derm of the skin which gives rise to the stroma of squamous epithelioma. Cylindrical epithelioma metastasizes slowly, and the secondary metastatic nodules in internal organs reproduce the columnar type of the parent structure. In malignancy and metastasis the cylindrical epithelioma resembles more closely the glandular carcinoma than the squamous epithelioma.

GLANDULAR CARCINOMA

Definition.—Glandular or medullary cancers are malignant, metastatic, epithelial neoplasms which resemble racemose glands in arrangement. They are the most malignant and most widely distributed variety of cancers in humans and in domestic animals. Statistics show cancer to be on the increase, not only in man, but also in domestic animals.

Nature and structure.—Medullary cancers, like surface carcinomas, consist of an epithelial parenchyma and a connective-tissue stroma or matrix. The parenchyma of glandular cancers forms continuous branching cylindrical masses of proliferating epithelial cells which extend in various planes. These masses in sections appear as alveolar spaces filled with epithelium obliterating the lumen, proliferating into the surrounding tissue. The cells in cancers differ in shape, size, and structure, depending on the kind of gland from which they originated, the pressure exerted by the stroma, and the amount of nutrition which the cells receive. These structural differences are sufficient reason why a single cell isolated from a cancer does not convey characteristics enough to identify it as a cancer cell. In fact that cell could have come from a papilloma, an adenoma, or a normal racemose gland.

The alveolar walls are composed of connective tissue which supports the blood vessels and lymph vessels to supply the nutrition to the neoplasms. The fibrous-tissue stroma may be scanty or abundant. When the stroma is scanty the parenchyma forms large cancer nests; the neoplasm is soft to the touch and is generally known as encephaloid, medullary, or soft cancer. If the stroma is abundant and the connective tissue densely arranged the cancer is hard to the touch and is known as scirrhous or hard cancer. The cancer nests in the hard cancer are small, indicating that the epithelial cell proliferation is very inactive. Soft cancer develops in well-nourished subjects, whereas hard cancer grows in emaciated subjects.

The rapidity of the growth of cancers appears to be influenced by the state of nutrition which governs the specific "tissue reaction." Soft cancers grow more rapidly, as the tissue reaction is diminished in consequence of a smaller amount of connective-tissue stroma present, when less resistance is offered to the epithelial-cell proliferation. Hard cancer, on the other hand, grows very slowly, as the tissue reaction appears to be increased in the emaciated subject where the

excessive connective-tissue development increases the resistance by retarding at the same time the epithelial-cell proliferation.

Besides the variation in the amount of connective tissue in the stroma of cancers, ranging from a mere scantiness to a conspicuous abundance of fibrous tissue, the stroma may undergo hyaline or myxomatous degeneration and become gelatinous in appearance. The stroma at times is very cellular, when the cancer is known as sarcomatous carcinoma, which is not a good term.

Appearance.—For a time a cancer is limited to the gland from which it has originated and is known as primary cancer. Cancers do not remain long in an inactive state. They are not encapsulated and the epithelial cells proliferate and penetrate into the surrounding tissues in the direction of least resistance, which is the course of the lymph vessels. It is not possible, on macroscopic inspection, to define the limits of the cancer from the surrounding tissues. Microscopic examination alone can determine the exact limits of the cancer invasion. When the cancer has existed for some time the nodular condition becomes more apparent. On section a whitish milklike seroalbuminous fluid exudes, which is generally called cancer juice. The ill-defined limits of cancer invasion necessitate total extirpation of the neoplasm and a generous amount of the adjacent and apparently unaffected tissue to avoid recurrence of the growth.

Secondary metastatic deposits in internal organs and tissues are sharply circumscribed nodes which stand out in great contrast from the affected part. The nodes are generally multiple, have a tendency to reach to the periphery, and often become umbilicated in the center. This is particularly the case with cancer nodes in the liver, spleen, and lungs. In the kidneys the nodules may be so numerous and so extensive as to convert the entire organ into a shapeless mass which has been known to weigh as much as 15 kilograms.

Clinical observations have shown that metastases may be extensive or limited. The extensive metastatic invasions are found in cases of soft cancer, which always grows rapidly, but in cases of hard cancer the metastasizing property is limited in extent and slow to start. The lymph vessels are the principal channels for the transmission of secondary metastatic deposits in cancer, while in sarcoma metastasis takes place essentially by the blood vessels. As in sarcoma (lymph sarcoma), metastasis may take place by a different route, the lymph vessels, so in carcinoma, when the neoplasm occurs in the stomach or the intestine the cell proliferation may be so close to a blood vessel as to admit some of the epithelial cells into the blood current to be carried to other tissues.

Seats.—The common seats for medullary cancers are the pyloric ends of the stomach, the mammary gland, uterus, intestine, liver, pancreas, kidneys, lung, ovaries, and testicles. As secondary metastatic deposits carcinoma may be found in lymph glands, and when the emboli gain entrance into the circulation the cancer may develop in any tissue where the emboli become lodged.

Though the usual way of cancer transmission is by the lymph vessels, less frequently by the blood vessels, it may very rarely be transferred by an eruption on a peritoneal surface. These infections result from peritoneal rupture and separation of detached cells in cancers of the uterus and of the gall bladder. The lesion results

either in miliary carcinomatosis of the peritoneal cavity or a generalized deposit of cancer nodules, which are more of the nature of plastic masses and frequently become confluent.

Age as a diagnostic factor.—In human cases the age of the subject has considerable diagnostic value, as it has been found that cancer usually occurs after middle age, and that malignant neoplasms in the young are almost invariably sarcoma. These facts are of great interest, as they have some bearing on the frequency of cancers in domestic animals. Statistics show that medullary cancers are fairly frequent in the glands of aged dogs and mares, whereas in bovines, most of which are usually killed at an early age, medullary cancer is rare, while sarcomas are more common. Carcinomas are probably as frequently found in aged cattle and sheep as in horses.

COMBINATIONS OF CARCINOMA

Combinations.—Carcinoma frequently combines with adenoma to form adenocarcinoma. This is the most common combination. Opinions differ as to whether these neoplasms were originally adenomas which in the course of growth had proliferation and in which detachment of the lining cells led to the accumulation of these cells in the interior of the acini, resulting in the formation of cancer nests, or whether they started as glandular cancer, with a limited number of rows of cells, and as a result of degeneration and accumulation of serous fluid the rows of cells separated, resulting in a structure resembling disorganized acini of glands.

Vascular changes in carcinomas are frequent, when the neoplasms are known as angiocarcinomas or telangiectatic carcinomas.

Degeneration.—Colloid cancer is often described as a special form of cancer. It is more appropriate to call this alteration a gelatinous change, as in most cases the entire structure, stroma as well as parenchyma, is changed into a substance resembling jelly, which is in reality a retrogressive mucous degeneration. Very rarely a true colloid degeneration affects the epithelial parenchyma; when such change does occur it is usually in neoplasms of the thyroid gland. Cancers of the stomach, mammary gland, and intestines are affected more often by mucous degeneration than by colloid.

Suppuration is very common in all forms of cancer, especially when they are exposed to infections of pathogenic microorganisms inducing a septic condition in the body. The products of septic microorganisms are toxins which are absorbed into the blood stream, producing a general disturbance known as cancerous cachexia.

Infection.—Clinical observations show that cancers of the mammary glands are invariably sterile unless surface ulceration has set in, which sometimes occurs in advanced stages. Some of the cancers, as those of the lip, tongue, esophagus, and especially those of the uterus, intestine, and rectum, harbor excessive numbers of microorganisms. Such cancers are usually called infectious cancers. It is therefore important to bear in mind that long-protracted, chronic cases of cancer may terminate in death by terminal infection, which may result in uremia, pneumonia, meningitis, or peritonitis, and is due to the toxins formed by the multiplication of microorganisms that infect the cancer. Infectious cancers often resemble chronic

inflammation of the lymp vessels and glands so closely that it requires a microscopic examination to tell them apart.

DISTINCTION BETWEEN CARCINOMA AND SARCOMA

According to the histogenetic classification of neoplasms, a sharp line of distinction exists between sarcomas, which are mesoblastic or of connective-tissue origin, and carcinomas, which are of epiblastic or epithelial origin. As a matter of fact, however, certain neoplasms which are classed as sarcomas (alveolar) show a histological structure which resembles carcinoma so closely that in a single slide and without the history it is difficult to distinguish one from the other.

Transplantation experiments of carcinoma in mice have shown that carcinomas become changed into sarcomas after 12 or 14 successive generations of transplantation.

Some of the textbooks on pathology have tables of the diagnostic features of sarcoma and carcinoma. The following points may be helpful in distinguishing between sarcoma and carcinoma:

Sarcoma	Carcinoma
1. Origin.—Mesoblast (connective tissue).	Epiblast or hypoblast and mesoblast (both epithelium and connective tissue).
2. Cells.—Embryonal connective-tissue cells.	Epithelial cells contained in alveoli, varying in shape and size.
3. Intercellular substance.—May be present.	Absent, or merely fluid.
4. Stroma.—Intercellular stroma rarely forms alveoli.	Connective tissue forms communcating alveoli in the course of lymphatics.
5. Blood supply.—Vessels are embryonic, often mere channels in contact with the cells. No muscle in the walls.	Vessels well developed, contained within and supported by the walls of the alveoli. Seldom in contact with the cells. Have distinct muscle walls.
6. Metastasis.—Ordinarily by blood vessels, exceptionally by lymph vessels.	Usually by lymph vessels, but in later stages also by blood vessels.
7. Malignancy.—Marked.	Very marked.
8. Usual seats.—Primary sarcoma is generally found in connective tissues, as corium, fasciæ, periosteum, brain, ovary, rarely in liver, lung, and uterus. Occurs primarily in lymph glands but not by metastasis.	Primary cancers occur on epithelial surfaces and in glands, especially on the lips, in mammary gland, stomach, intestines, uterus, vagina, and penis. Can be carried to any tissue by metastasis. Does not occur primarily in lymph glands but is usually present secondarily.
9. Sensitiveness.—Usually not painful.	Always painful.
10. Age.—Occurs usually in the young.	Generally occurs in middle life or later.
11. Growth.—Often interrupted.	Continuous, often rapid.
12. Shape.—Often rounded, fleshlike masses.	Nodular, tubular, dendritic, often ulcerating on surface.
13. Heredity.—Rarely hereditary.	Often hereditary.
14. Secondary changes.—Myxomatous degeneration common. Calcification and pigmentation very common. Ossification and condroid not so common. No fat within the neoplasm.	Fatty degeneration very common, almost from the start. Mucocolloid frequent. Pigmentation rare. Cystic change rare. Fat may be present within the cancer tissue.

TERATOID NEOPLASMS (TERATOMA)

Teratomas comprise a group of neoplasms containing heterogeneous tissue elements of one or several mature tissues or organs, and seem to be derived from all three layers of the embryo. They are always of congenital origin and are usually cystic in nature. Dermal structures are the prominent feature comprising skin, muscle, cartilage, bone, teeth, hair, also nerve tissue, and even certain of the viscera. The dermal tissues invariably predominate; hence the name dermoid is generally used, and as the process is always accompanied by cystic change, the name dermoid cyst is used. When the cystic change is lacking and reproduction of the viscera and other peripheral structures resemble fetal parts the growth is termed congenital malformation or monstrosity. Some pathologists include in this group the so-called mixed neoplasms of congenital origin which have been previously mentioned as combinations of neoplasms.

Dermoid cysts occur in man and are not uncommon in domestic animals.

DERMOID CYST

Small dermoid cysts occur frequently in dogs, horses, and cattle, in the order named. Not infrequently they are found in sheep and hogs. It is interesting to note that the hair fibers in the dermoid cysts in sheep resemble wool, whereas the fibers in the dermoid cysts of hogs resemble bristles, and the dermoids in birds frequently contain feathers. In humans (children) small dermal nodes occurring on the face are described by the name mandibular tubercles. In many mammals, especially dogs, similar mandibular tubercles or cutaneous nodes have been recorded.

The most common place for dermoid cysts is the ovary. Some writers describe them by the name cystic embryomas. Less frequently are dermoid cysts found in the testicle. They are also found in the thoracic cavity, in the abdominal cavity, starting behind the peritoneum, involving the kidney, in the mesentery, and in the omentum. Dermoid cysts are occasionally found in the mammary gland, in the parotid gland, about the eyeball, on the head at the junction of the cranial bones, on the face, and on the neck.

Dermoid cysts in the ovary, like those occurring elsewhere, are lined with epithelium. They generally contain hair, teeth, or other dermal tissues, and are filled with fluid, which may be clear or cloudy. The cyst contents may also be gelatinous, mucous, fatty, or sebaceous in nature. Microscopic sections show the structure of skin, hair follicles with hair, sebaceous and sweat glands, developing and adult teeth, pharyngeal mucous membrane, intestine, and thyroid gland. Wilms reports finding traces of nerve tissue in ovarian cysts.

Most dermoid cysts are benign and grow slowly, but some of them are malignant and grow as rapidly as any malignant neoplasm, give metastasis, and recur after removal.

Some cysts in the ovary are not congenital, and are described as simple cysts or cystadenomas. They are covered by a connective-tissue capsule and are lined by columnar epithelium. Such cysts are variable in size, may become very large, and contain a thin, watery

fluid, or the fluid may be thick and viscid. Neither the walls nor the interior contain any dermal structure.

CYSTS

Cysts (not dermoid) are circumscribed, encapsulated, or walled-in cavities containing an abnormal accumulation of fluid or semi-fluid substance and not provided with an outlet. The term is often very loosely used by some writers. Cysts are generally classed with neoplasms, but this is more for convenience and not by reason of structural or etiological similarity, as cysts stand midway between neoplasms and dermoid cysts. Cysts are described as simple or unilocular when the cyst wall is passive, serving only to retain the contents. When several cysts occur together and are identical in structure, arising from the same cause, they are called multiple cysts, or when the cysts spring from the inside wall of a cyst they are spoken of as multilocular cysts.

According to the method of formation, cysts may be classified as retention cysts, exudation cysts, extravasation cysts, softening cysts, and parasitic cysts.

Retention cysts arise from the accumulation of secretion when the duct of a gland has been occluded, preventing the escape of the secretion. The most common cysts are the sebaceous cysts of the skin, called wens, the mucous salivary gland cysts of the tongue, called ranula, the pancreatic cysts, the galactoceles (milk cysts) in the mammary glands, etc. The cyst contents are derived from the functional activity of the glands and are eventually altered by absorption of some of the fluid and by the subsequent degenerative changes that affect the fluid as well as the lining and the walls of the cyst. These degenerative changes may bring about an irritation that gives rise to inflammation.

Exudation or distention cysts resemble so closely the retention cysts that many writers make no distinction between them. They are cysts which occur in closed cavities not supplied by an excretory duct, as in hydrocele that may be found in the tunica vaginalis testis, or cysts in the ovaries. The distention of enlarged bursæ occurring in the elbow and the hock in horses as pouchlike dilations and the cysts found in the course of tendons are retention cysts and are known as windgalls. The dilated spaces forming cysts in the thyroid gland and the pituitary gland may be classed with the retention or with the exudation cysts.

Extravasation or hemorrhagic cysts are the result of blood escaped from a vessel into a tissue or an organ. They are known as hematocele or sanguineous cysts. They become eventually surrounded by a capsule, which varies in thickness in different organs. Such cysts are common in domestic animals and are generally the result of traumatism, or they may result from rupture due to disease in the walls of a blood vessel.

Softening cysts are pathological cavities which result from disintegration of solid tissues by retrograde changes and liquefaction necrosis. Such cysts may be found in rapidly growing neoplasms, especially in sarcomas and carcinomas in which myxomatous degeneration has taken place. Colloid and mucoid degeneration finally terminates in the formation of softening cysts. Some writers also

class the hemorrhagic cysts, especially those occurring in the brain, among the softening cysts. It must be remembered that some hemorrhagic cysts may undergo regeneration instead of softening.

SYNCYTIOMA

Syncytioma (chorion carcinoma, chorioepithelioma, deciduoma, placentoma) is a malignant neoplasm, soft, friable, and spongy in structure, dark in color, generally containing blood clots. The neoplasm resembles placental tissue in appearance and structure. It originates during or after pregnancy and sometimes follows abortion. Recent observations have shown that it may be the result of teratomatous or embryomatous growth, as it has been found as testicular teratoma or embryoma, also as a mediastinal and cranial teratoma. The neoplasm is most malignant and generally gives metastasis to the external genitalia and less frequently to the liver, kidney, spleen, or other organs.

Syncytioma has not been described in domestic animals.

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